Regulated beta-cell regeneration in the adult mouse pancreas.

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Public Summary:

Scientific Abstract:
Several studies have shown that the adult pancreas possesses a limited potential for beta-cell regeneration upon tissue injury. One of the difficulties in studying beta-cell regeneration has been the lack of a robust, synchronized animal model system that would allow controlled regulation of beta-cell loss and subsequent proliferation in adult pancreas. Here we present a transgenic mouse regeneration model in which the c-Myc transcription factor/mutant estrogen receptor (cMycER(TAM)) fusion protein can be specifically activated in mature beta-cells. We have studied these transgenic mice by immunohistochemical and biochemical methods to assess the ablation and posterior regeneration of beta-cells. Activation of the cMycER(TAM) fusion protein results in synchronous and selective beta-cell apoptosis followed by the onset of acute diabetes. Inactivation of c-Myc leads to gradual regeneration of insulin-expressing cells and reversal of diabetes. Our results demonstrate that the mature pancreas has the ability to fully recover from almost complete ablation of all existing beta-cells. Our results also suggest the regeneration of beta-cells is mediated by replication of beta-cells rather than neogenesis from pancreatic ducts.